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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|----------------------|----------------------|---------------------|------------------|
| 10/609,383 | 07/01/2003 | Richard J. Feldmann | 3279-Z | 4498 |
| | 7590 01/23/200° | 7 | EXAM | INER |
| Law Office of Jim Zegeer Suite 108 801 North Pitt Street Alexandria, VA 22314 | | BRUSCA, JOHN S | | |
| | | | ART UNIT | PAPER NUMBER |
| , | | | 1631 | |
| SHORTENED STATUTOR | Y PERIOD OF RESPONSE | MAIL DATE | DELIVER | Y MODE |
| 3 MONTHS 01/23/2007 PAPER | | ER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| | | | Application No. | | Applicant(s) | |
|--|---|--|--|---|--------------------------------------|-------------|
| Office Action Summary | | | 10/609,383 | | FELDMANN, RIC | HARD J. |
| | | Examiner | | Art Unit | - | |
| | | | John S. Brusca | | 1631 | |
| Period fo | The MAILING DATE of this commun or Reply | ication app | ears on the cover st | neet with the co | orrespondence ad | ldress |
| WHIC - Exter after - If NO - Failu Any | ORTENED STATUTORY PERIOD F CHEVER IS LONGER, FROM THE M Issions of time may be available under the provisions SIX (6) MONTHS from the mailing date of this comm or period for reply is specified above, the maximum state to reply within the set or extended period for reply reply received by the Office later than three months are patent term adjustment. See 37 CFR 1.704(b). | IAILING DA of 37 CFR 1.13 nunication. atutory period w will, by statute. | ATE OF THIS COMI 36(a). In no event, however rill apply and will expire SIX cause the application to be | MUNICATION , may a reply be time (6) MONTHS from the | ely filed the mailing date of this c | • |
| Status | • | | | | | |
| 1)[🛛 | Responsive to communication(s) file | ed on 04 De | ecember 2006 and | 22 Santambar | 2006 | |
| · — | | | action is non-final. | <u> 22 Oeptember</u> | <u>2000</u> . | |
| 3) | Since this application is in condition | • | | al matters pros | secution as to the | e morite is |
| ٠,- | closed in accordance with the practi | | | • | | o mento io |
| D:i4: | | | pario Quayro, 100 | | J 0.0. 210. | |
| · | on of Claims | | | | | • |
| | Claim(s) 1-12 is/are pending in the a | • • | | | • | |
| | 4a) Of the above claim(s) <u>3-12</u> is/are | withdrawn | from consideration | | | |
| 5)[_] | Claim(s) is/are allowed. | | | | | |
| 6)⊠ | 6)⊠ Claim(s) <u>1 and 2</u> is/are rejected. | | | | | |
| 7) | Claim(s) is/are objected to. | | | | ٠ | |
| 8)□ | Claim(s) are subject to restrict | tion and/or | election requireme | nt. | | |
| Applicati | on Papers | | | | • | |
| 9)🖾 🤄 | The specification is objected to by the | e Examine | ŕ. | | | |
| 10)[| The drawing(s) filed on is/are: | a) acce | epted or b) 🗀 object | ed to by the E | xaminer. | |
| | Applicant may not request that any object | | · · | - | | |
| | Replacement drawing sheet(s) including | | | | | FR 1.121(d) |
| 11)[| The oath or declaration is objected to | | | | | |
| | nder 35 U.S.C. § 119 | • | | | | |
| 12)□ | Acknowledgment is made of a claim | for foreign | priority under 35 LL | S.C. & 110(a) | (d) or (f) | |
| _ | ☐ All b)☐ Some * c)☐ None of: | ioi ioroigii | priority drider 55 C. | 0.0. g 119(a)- | (d) or (i). | |
| -/. | | documents | have been receive | .d | | |
| | 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No | | | | | |
| | 3. Copies of the certified copies | | | | | 04 |
| • | application from the Internatio | | | | ın this National | Stage |
| * \$ | ee the attached detailed Office actio | | • | • | • | |
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| Attachment | (s) . | | | | | |
| I) 🔀 Notice | Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) | | | | | |
| 2) Notice | e of Draftsperson's Patent Drawing Review (P | TO-948) | Pap | er No(s)/Mail Date | е | |
| B) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 5) ☐ Notice of Informal Patent Application 6) ☑ Other: Notice to Comply. | | | | | | |

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DETAILED ACTION

Priority

1. The applicant's claim for benefit of Provisional U.S. Application No. 60/393558 is accepted in view of the amendment to the specification filed 22 September 2006.

Information Disclosure Statement

- 2. The information disclosure statement filed 19 November 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.
- 3. The applicants have filed a CD-ROM with references in lieu of a paper copy, however foreign and non-patent references must be submitted as paper copies. At this time the Office has no provisions to accept references on a CD-ROM.
- 4. The Information Disclosure Statement filed 19 November 2003 does not contain a paper copy of each reference listed on the list of references as discussed above. If the applicants provide a legible copy of the missing references in response to this Office action, the references will be considered under 37 CFR 1.97(f), and a signed copy of the list of references indicating consideration of the missing references will be provided to the applicants without the necessity of the applicants filing a second Information Disclosure Statement.
- 5. Applicant's arguments filed 22 September 2006 have been fully considered but they are not persuasive. The applicants state that a CD-ROM should be considered to be a legible copy,

however the Office at present does not accept CD-ROMs as meeting the requirement of a legible copy of cited references in an information disclosure statement.

Specification

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the following reasons:

SEQ ID NOS have been added to the specification in response to the objection to the specification in the Office action mailed 22 March 2006, however the computer readable form associated with the new sequence listing is defective. Please see the Notice to comply and RSL error report attached to this Office action.

Claim Rejections - 35 USC § 112

- 7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
 - The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 8. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or

absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

- a) Quantity of experimentation: The only utility asserted by the specification is to use connectron symmetries to predict control of gene expression (see for example pages 11, 15, and 16 of the specification). In order to practice the claimed invention one of skill in the art must identify and use a connectron to predict regulation of gene expression. In some embodiments changes in connectron behavior that correlate with changes in gene expression is monitored or effected. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.
- b) The amount of direction or guidance presented: The claimed invention is a method of identification of sequences that have a connectron relationship and act to modulate gene expression. On page 3, the specification defines connectrons as a tetradic structure between two sequences in an RNA transcript of a genomic sequence and two sequences in double stranded genomic DNA. The specification speculates without evidence on page 7 that triple-stranded (triplex) structures will form between RNA and double stranded DNA in chromatin where connectron symmetries are identified. The specification does not provide guidance that there are any limitations on formation of triplex structures, and only implies that regions of RNA with identical sequence to one strand of a double stranded DNA sequence will form triplex structures. The specification does not address why all RNA transcripts of genes would not form a continuous triplex structure with the gene from which it is transcribed. The specification provides guidance to identify connectron symmetries in genomic sequences. The specification

does not provide detailed guidance to use identified connectron symmetries because the specification does not show whether or not connectrons form within cells or have an effect on gene expression. The specification does not provide specific guidance for monitoring or effecting changes in connectron behavior that correlate with gene expression.

- c) The presence or absence of working examples: The specification provides working examples of identification of connectron symmetries by computer-mediated searching of genomic sequences. However, the specification does not provide evidence that connectron symmetries in genomic sequences result in formation of triplex RNA-DNA structures or that if connectron triplex structures do exist that connectrons control gene expression. The specification does not provide working examples of using identified connectron symmetries to predict effects on gene expression. The specification does not provide working examples of monitoring or effecting changes in connectron behavior that correlate with gene expression.
- d) The nature of the invention: The nature of the invention, gene expression control, is complex.
- e) The state of the prior art: One of skill in the art, after reading the specification, would not know that connectron symmetries identified by computer-mediated searches of genomic sequences would allow for prediction of gene expression of genes that have connectron symmetries. The specification does not provide experimental evidence that connectron symmetries cause modulation of gene expression. Neither the prior art nor post-filing art shows connectrons. Mattick (published in 2001, one year after the effective instant filing date) reviews effects of RNA molecules on gene regulation. Mattick does not show connectrons as defined in the instant specification. Chan et al. reviews triplex DNA formation. Chan et al. shows in figures

1A-C that short stretches of oligonucleotides may form parallel or antiparallel triplex structures. Chan et al. shows in figures 1B that parallel triplex forming oligonucleotides form bonds between C and T residues of the oligonucleotide and G and A residues of the double stranded DNA molecule. Figure 1C shows that antiparallel triplex forming oligonucleotides form bonds between A, G, and T residues of the oligonucleotide and A, G, and A residues of the double stranded DNA. Chan et al. characterize the limited range of base pairing possibilities in triplex structures as pyrimidine binding motifs or purine binding motifs. Chan et al. describe on pages 268-273 the unpredictability and difficulty of forming desired triplex structures that are limited to the purine motif or the pyrimidine motif. Chan et al. does not show a mechanism that allows for triplex structures to form with any and all regions of identity between an RNA transcript and a region of double stranded DNA that has an identical sequence in one of the two strands of DNA, as required for connectron formation as defined in the instant specification.

- f) The relative skill of those in the art: The skill of those in the art of gene expression is high.
- g) The predictability of the art: The predictability of the relationship of connectron symmetries and gene expression is unknown in the prior art and is not described in the instant specification.
- h) The breadth of the claims: The claims are broad in that they are drawn to identification and modulation of connectron symmetries whose relationship to gene expression is not established.

The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the specification lacks any evidence that connectrons form in

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cells or that connectron symmetries are related to gene expression. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss connectron symmetries. Chan et al. shows that triplex formation occurs only with oligonucleotides with a purine rich or pyrimidine rich motif, rather than with any identical sequence as suggested in the specification. Finally, said practitioner would turn to trial and error experimentation to determine a relationship between connectron symmetries and gene expression. Such amounts to undue experimentation.

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9. Applicant's arguments filed 22 September 2006 have been fully considered but they are not persuasive. The applicants state that one of skill in the art would be able to determine connectron symmetries by analysis of genomic sequence data. However, although the specification provides guidance and working examples of determining connectron symmetries in genomic data, the specification does not enable one of skill in the art to use connectron symmetries to predict regulation of gene expression because the specification does not show that connectron symmetries have any relationship to triplex formation or control of gene expression in cells, and the only utility asserted by the specification is to use connectron symmetries to predict control of gene expression (see for example pages 11, 15, and 16 of the specification).

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

John S. Brusca Jonnay 2007

Primary Examiner
Art Unit 1631

Page 8

NOTICE TO COMPLY WITH SEQUENCE RULES

| Application No. | Applicant(s) | |
|-----------------|-------------------|--------------|
| 10/609,383 | FELDMANN, RICHARD | J . , |
| Examiner | Art Unit | |
| John S. Brusca | 1631 | |

| | John S. Brusca | 1631 | |
|---|----------------------------------|-----------------|----------------|
| NOTICE TO COMPLY WITH REQUIREMEN | | | AINING |
| NUCLEOTIDE SEQUENCE AND/OR AMINO | | | |
| The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821-1.825 for the following reasons: | | | |
| 1. This application clearly fails to comply with the requirements of 37 CFR 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990. | | | |
| 2. This application does not contain, as a separa as required by 37 CFR 1.821(c). | te part of the disclosure on pap | er copy, a "Seq | uence Listing" |
| 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e). | | | |
| 4. A copy of the "Sequence Listing in computer readable form has been submitted. However the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked up "Raw Sequence Listing". | | | |
| 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable. A Substitute computer readable form must be submitted as required by 37 CFR 1.825(d). | | | |
| 6. The paper copy of the "Sequence Listing" is null building as required by 37 CFR 1.821(e). | ot the same as the computer re | eadable form of | the "Sequence |
| ☐ 7. Other: | | | |
| Applicant must provide: | | | |
| ☐ An initial or ☒ A substitute computer readable | form copy of the Sequence Li | sting. | |
| An initial or A Substitute paper copy of the Sequence Listing as well as an amendment directing its entry into the specification. | | | |
| A statement that the content of the paper and computer readable copies are the same, and, where applicable, include no new matter, as required by 37 CFR 1.821(e), (f), or (g) or 1.825(b) or (d). | | | |
| FOR QUESTIONS PLEASE CONTACT: | • | | |
| Rules Interpretation (703) 308-4216 CRF Submission Help (703) 308 4212 PatentIn software help (703) 308 6856 | | | |
| | • | | |

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: /0/609, 383/3
Source: /Fw/b

Date Processed by STIC:

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER</u> <u>VERSION 4.4.0 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

- 1. EFS-Bio (http://www.uspto.gov/ebc/efs/downloads/documents.htm, EFS Submission User Manual ePAVE)
- 2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
- Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):
 U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

| ERROR DETECTED | SUGGESTED CORRECTION SERIAL NUMBER: 10/6.09, 383B |
|-------------------------------------|--|
| ATTN: NEW RULES CASES | : PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE |
| lWrapped Nucleics Wrapped Aminos | The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping." |
| 2Invalid Line Length | The rules require that a line not exceed 72 characters in length. This includes white spaces. |
| 3Misaligned Amino Numbering | The numbering under each 5 th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead. |
| 4Non-ASCII | The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text. |
| 5Variable Length | Sequence(s)contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing. |
| 6PatentIn 2.0 "bug" | A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences. |
| 7Skipped Sequences (OLD RULES) | Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences. |
| 8Skipped Sequences (NEW RULES) | Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence. <210> sequence id number <400> sequence id number 000 |
| 9Use of n's or Xaa's (NEW RULES) | Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents. |
| 10 V Invalid <213> Response | Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence. (see item 11 below) |
| Use of <220> | Sequence(s) missing the 220 "Feature" and associated numeric identifiers and responses Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown" Please explain source of genetic material in <220> to <223> section or use "chemically synthesized" as explanation. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32), also Sec. 1.823 of Sequence Rules |
| Patentin 2.0 "bug" | Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk. |
| 13 Misuse of n/Xaa | "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid |



IFW16

RAW SEQUENCE LISTING DATE: 09/27/2006 PATENT APPLICATION: US/10/609,383B TIME: 15:13:28

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Output Set: N:\CRF4\09272006\J609383B.raw

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65 ctttggttac cgtgacatcc tgcgaatctc atgtgtgcac tgaatc

166

DATE: 09/27/2006

TIME: 15:13:28

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RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/609,383B

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DATE: 09/27/2006

TIME: 15:13:28

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                     Output Set: N:\CRF4\09272006\J609383B.raw
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     150 <222> LOCATION: (757718)...(757753)
     151 <223> OTHER INFORMATION: Chromosome = 1 Strand = negative ConnectronObjectNumber =
975
     154 <400> SEQUENCE: 9
     155 ttacgcctga tgcgctgcgc ttatcaggcc tacggg
                                                                                       36
     158 <210> SEQ ID NO: 10
     160 <211> LENGTH: 16
     161 <212> TYPE: DNA
     162 <213> ORGANISM: Saccharomyces cerevisiae complete genome - problem.
     164 <220> FEATURE:
     165 <222> LOCATION: (221330)...(221345)
     166 <223> OTHER INFORMATION: Chromosome = 2 Strand = positive ConnectronObjectNumber =
792a
     169 <400> SEQUENCE: 10
     170 tatatatatg tcactg
                                                                                       16
     173 <210> SEQ ID NO: 11
     175 <211> LENGTH: 16
     176 <212> TYPE: DNA
     177 <213> ORGANISM: Saccharomyces cerevisiae complete genome - problem.
     179 <220> FEATURE:
     180 <222> LOCATION: (221346)...(221361)
     181 <223> OTHER INFORMATION: Chromosome = 2 Strand = positive ConnectronObjectNumber =
793
     184 <400> SEQUENCE: 11
     185 tattgcatgc tggatg
                                                                             16
     188 <210> SEQ ID NO: 12
     190 <211> LENGTH: 539
     191 <212> TYPE: DNA
     192 <213> ORGANISM: Saccharomyces cerevisiae complete genome - problem.
     194 <220> FEATURE:
     195 <222> LOCATION: (448454)...(448992)
     196 <223> OTHER INFORMATION: Chromosome = 5 Strand = positive ConnectronObjectNumber =
4749
     199 <400> SEQUENCE: 12
     200 tatatatatg tcactgtatt gcatgctgga tggtgttaga caaggccgta gggacatata
                                                                                       60
     201 gcatctagga agtaaccttg tacgaaaata ggcaatattt
                                                        cctgtttagg cgattgtgac
                                                                                      120
     202 gcagatttta gtccaacgat ctagcgtcaa ggaatttttt tatagtggga cattgcacca
                                                                                      180
     203 aggaagtaac ttgatacgtc gtgggtgaat gggtctgttt
                                                         tcttattcgg
                                                                     cggggtaata
                                                                                      240
     204 catttttggg ggaagtttgt
                                ctgtctgacg cgccatatgt
                                                         aggtacgcca
                                                                     aaaagggctc
                                                                                      300
     205 ctctacttcg aagcgcgagg tcgtatacct aataaggaaa
                                                         tgtaatttat
                                                                     aactttttat
                                                                                      360
     206 tatattggtc ttttcgagag cggaacgtag
                                            gtccatgttt
                                                         aaagtatcca
                                                                                      420
                                                                     agagaatatc
     207 cacgaagcgg
                                aacagaatcc
                    ctgagcaacg
                                             tggttctcct
                                                         cgactaagca
                                                                                      480
                                                                     gatagttaag ·
     208 atactgtgca ccatggaaat
                                tgaaaacgaa agtacgtacc
                                                         gactacttta tttttgcag
                                                                                      539
     210 <210> SEQ ID NO: 13
     212 <211> LENGTH: 158
     213 <212> TYPE: DNA
     214 <213> ORGANISM: Saccharomyces cerevisiae complete genome - problem.
     216 <220> FEATURE:
     217 <222> LOCATION: (24863)...(25028)
    218 <223> OTHER INFORMATION: Chromosome = 5 Strand = negative ConnectronObjectNumber =
4824a
     221 <400> SEQUENCE: 13
```

RAW SEQUENCE LISTING

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222 tatatatatg tcactgtatt gcatgctgga tggtgttaga caaggccgta gggacatata

60

DATE: 09/27/2006

PATENT APPLICATION: US/10/609,383B TIME: 15:13:28 Input Set : F:\synthetic.txt Output Set: N:\CRF4\09272006\J609383B.raw 223 gcatctagga agtaaccttg tacgaaaata ggcaatattt cctgtttagg cgattgtgac 120 224 gcagatttta gtccaacgat ctagcgtcaa ggaatttt 158 226 <210> SEQ ID NO: 14 228 <211> LENGTH: 134 229 <212> TYPE: DNA 230 <213> ORGANISM: Halobacterium sp. NRC-1 complete genome. 232 <220> FEATURE: 233 <222> LOCATION: (732401)...(732534) 234 <223> OTHER INFORMATION: Chromosome = 1 Strand = positive ConnectronObjectNumber = 6612 237 <400> SEQUENCE: 14 238 ttcatcacag acgaggacga gcgcggccaa gtggggatcg gcacactcat cgtgttcatc 60 239 gcgatggtgc tggtcgccgc gatcgccgcc ggcgtcctca tcaacactgc cggctacctc 120 240 caatccaagg ggtc · 134 243 <210> SEQ ID NO: 15 245 <211> LENGTH: 193 246 <212> TYPE: DNA 247 <213> ORGANISM: Halobacterium sp. NRC-1 complete genome. 249 <220> FEATURE: 250 <222> LOCATION: (733018)...(733209) 251 <223> OTHER INFORMATION: Chromosome = 1 Strand = positive ConnectronObjectNumber = 6644a 254 <400> SEQUENCE: 15 255 gacgagcgcg gtcaagtggg gatcggcaca ctcatcgtgt tcatcgcgat ggtgctggtc 60 256 geogegateg cegeeggegt ceteateaac acegeegget acetecaate caaggggteg 120 257 gcaaccggtg aggaagcete egcacaggte tecaaccgca teaacategt etcegegtae 180 258 ggcaacgtca aca 193 261 <210> SEQ ID NO: 16 263 <211> LENGTH: 85 264 <212> TYPE: DNA 265 <213> ORGANISM: Halobacterium sp. NRC-1 complete genome. 267 <220> FEATURE: 268 <222> LOCATION: (773399)...(773483) 269 <223> OTHER INFORMATION: Chromosome = 1 Strand = positive ConnectronObjectNumber = 6852 272 <400> SEQUENCE: 16 273 gtggggatcg gcacgctcat cgtgttcatc gcgatggtgc tggtcgccgc gatcgccgcc 60 274 ggcgtcctca tcaacactgc cggct 85 277 <210> SEQ ID NO: 17 279 <211> LENGTH: 121 280 <212> TYPE: DNA 281 <213> ORGANISM: Pseudomonas aeruginosa PA01, complete genome. 283 <220> FEATURE: 284 <222> LOCATION: (4832718)...(4832838) 285 <223> OTHER INFORMATION: Chromosome = 1 Strand = positive ConnectronObjectNumber = 53464 288 <400> SEQUENCE: 17 289 gccaacatcg aggccctcaa cagccgcacg gtgaacatcg gccagatcct cgaagtgatc 60 290 aagggcatet eegageagae caacetgete geeeteaaeg eegecatega ageegegege 120 291 g 121 294 <210> SEQ ID NO: 18 296 <211> LENGTH: 194 297 <212> TYPE: DNA

RAW SEQUENCE LISTING

RAW SEQUENCE LISTING DATE: 09/27/2006
PATENT APPLICATION: US/10/609,383B TIME: 15:13:28

Input Set : F:\synthetic.txt

Output Set: N:\CRF4\09272006\J609383B.raw

```
298 <213> ORGANISM: Pseudomonas aeruginosa PA01, complete genome.
     300 <220> FEATURE:
     301 <222> LOCATION: (4836528)...(4836720)
     302 <223> OTHER INFORMATION: Chromosome = 1 Strand = positive ConnectronObjectNumber =
53531
     305 <400> SEQUENCE: 18
     306 ggacggcaaa caggtggtcg agcagaccat ccgcgcgatg
                                                                                      60
                                                        aacgagcttt ccgagaagat
     307 cagegeetee tgegeeaaca tegaggeeet caacageege aeggtgaaca teggeeagat
                                                                                     120
     308 cctcgaagtg atcaagggca tctccgagca gaccaacctg ctcgccctca acgccgccat
                                                                                     180
     309 cgaagccgcg cgcg
                                                                                     194
     312 <210> SEQ ID NO: 19
     314 <211> LENGTH: 169
     315 <212> TYPE: DNA
     316 <213> ORGANISM: Pseudomonas aeruginosa PA01, complete genome.
     318 <220> FEATURE:
     319 <222> LOCATION: (4838678)...(4838846)
     320 <223> OTHER INFORMATION: Chromosome = 1 Strand = positive ConnectronObjectNumber =
53549a
     323 <400> SEQUENCE: 19
     324 accateegeg egatgaaega gettteegag aagateageg eeteetgege eaacategag
                                                                                      60
                                                                                     120
     325 geceteaaca geegeacggt gaacategge cagateeteg aagtgateaa gggeatetee
     326 gagcagacca acctgctcgc cctcaacgcc gccatcgaag ccgcgcgcg
                                 solid response. See item 10 on Ever Summary Sheet
     329 <210> SEQ ID NO: 20
     331 <211> LENGTH: 36
     332 <212> TYPE: DNA
     333 <213> ORGANISM: (Sequence Recognized by Synthetic DNA Binding Protein.
     335 <220> FEATURE:
     338 <400> SEQUENCE: 20
     339 tccccatgag catagatatg caggtaggcg gcaagt
     342 <210> SEQ ID NO: 21
     344 <211> LENGTH: 136
     345 <212> TYPE: DNA
     346 <213> ORGANISM: Vibrio cholerae chromosome I, complete chromosome.
     348 <220> FEATURE:
     349 <222> LOCATION: (952641)...(952777)
     350 <223> OTHER INFORMATION: Chromosome = 1 Strand = negative ConnectronObjectNumber =
607
    353 <400> SEQUENCE: 21
    354 tgtatatacc caaactactt ggagttgcag gtaggcggca agtgagtgag tccccatgag
                                                                                      60
     355 catagataga ctatgtgatt ggggtgaacg aacgtagcca acaccgctgc agcttcaagt
                                                                                     120
     356 aggaagggta tacctt
                                                                                     136
     359 <210> SEQ ID NO: 22
    361 <211> LENGTH: 117
    362 <212> TYPE: DNA
    363 <213> ORGANISM: Vibrio cholerae chromosome I, complete chromosome.
    365 <220> FEATURE:
    366 <222> LOCATION: (1005810)...(1005926)
    367 <223> OTHER INFORMATION: Chromosome = 1 Strand = negative ConnectronObjectNumber =
646
    370 <400> SEQUENCE: 22
    371 taccaaaact acttggagtt gcaggtaggc ggcaagagag tgaatcccca tcagcataga
                                                                                      60
    372 cagactatgt gattggggtg aacgaacgta gccaataccg ctgcagcttc aagtagg
                                                                                     117
    375 <210> SEQ ID NO: 23
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RAW SEQUENCE LISTING ERROR SUMMARY DATE: 09/27/2006
PATENT APPLICATION: US/10/609,383B TIME: 15:13:29

Input Set : F:\synthetic.txt

Output Set: N:\CRF4\09272006\J609383B.raw

Invalid Line Length:

The rules require that a line not exceed 72 characters in length. This includes spaces.

```
Seq#:1; Line(s) 27,28,29,30
Seq#:2; Line(s) 45,46,47,48
Seq#:3; Line(s) 63,64,65
Seq#:4; Line(s) 76,80
Seq#:5; Line(s) 95
Seq#:6; Line(s) 110
Seq#:7; Line(s) 121,125
Seq#:8; Line(s) 140
Seq#:9; Line(s) 155
Seq#:10; Line(s) 170
Seq#:12; Line(s) 200,201,202,203,204,205,206,207,208
Seq#:13; Line(s) 222,223,224
Seq#:14; Line(s) 238,239,240
Seq#:15; Line(s) 255,256,257,258
Seq#:16; Line(s) 273,274
Seq#:17; Line(s) 289,290,291
Seq#:18; Line(s) 306,307,308,309
Seq#:19; Line(s) 324,325,326
Seq#:20; Line(s) 339
Seq#:21; Line(s) 354,355,356
Seq#:22; Line(s) 371,372
Seq#:23; Line(s) 385
Seq#:24; Line(s) 400,401,402
Seq#:25; Line(s) 417,418
Seq#:26; Line(s). 425,431
Seq#:27; Line(s) 438,444
Seq#:28; Line(s) 459,460
Seq#:29; Line(s) 475,476,477
Seq#:30; Line(s) 489
Seq#:31; Line(s) 500
Seq#:32; Line(s) 511
Seq#:33; Line(s) 522
Seq#:34; Line(s) 533
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VERIFICATION SUMMARY

DATE: 09/27/2006

PATENT APPLICATION: US/10/609,383B

TIME: 15:13:29

Input Set : F:\synthetic.txt

Output Set: N:\CRF4\09272006\J609383B.raw

L:7 M:270 C: Current Application Number differs, Missing <140> CURRENT APPLICATION NUMBER: is

Added.

L:7 M:271 C: Current Filing Date differs, Replaced Current Filing Date